Reply to Slankamenac et al's Comprehensive Complication Index Validation Study (November 2014)

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Reply:

We greatly appreciate the positive interest by Dr O Boney, Dr R. Moonesinghe, and Professor M. Grocott in our article published in *Annals of Surgery* in November 2014.[1] We thank them for highlighting the important role and need for a composite endpoint for surgical complications such as the comprehensive complications index (CCI).[1,2]

Boney et al were interested in the methodology of the external validation of the CCI in 3 randomized controlled trials (RCT),[3–5] which were initially conducted for specific surgical complications as a primary endpoint and not for a composite endpoint. From a methodological point of view, it is not a problem to validate the CCI using RCTs which had different primary endpoints as long as all complications were ascertained. To ensure that we only relied on RCTs with high quality data on complications, we visited every center and assessed on site each postoperative complication in each patient, and then graded them according to the Clavien–Dindo classification.[6] With these visits, we ensured the completeness of complications and a harmonized approach to grade them across trials and to calculate the CCI.

Boney et al also raised the question if a composite endpoint is the best primary endpoint in RCT or not because it may mask important differences in specific complication rates. We are convinced that both the composite outcome measure and specific complications have advantages and disadvantages. This is exemplified by the trials comparing different surgical procedures or treatments. One patient group had a short-term advantage in terms of the primary outcome but that outcome did not consider the overall patient experience. Such focus on single endpoints is neglecting all other complications and likely to mask harms that contribute to the overall complications. The CCI as a composite complication score might indeed mask important differences in specific complication rates at different time points, but it has the advantage to reflect the overall burden of the postoperative course which is affecting the health of patients and their quality of life. Therefore, we recommend reporting both the single complications and the CCI to inform treatment decisions.[2]

Another comment by Boney et al discussed the minimal important difference of the CCI for determining the sample size for RCTs and for interpreting trial results. We greatly appreciate this important comment and essentially agree that it is difficult to conclusively determine the minimal important difference of the CCI. Because of the nonlinear nature of the CCI, it is unlikely that a 10-point difference applies across the range. Therefore, sample size calculations also require clinical judgment. Sometimes a 10-point difference is adequate whereas in other situations a smaller or larger difference of the CCI may be perceived important enough to change treatment decisions. It is important though to decide on the minimal important difference a priori and report it transparently.

Finally, we agree with Boney et al and also strongly recommend evaluating the CCI in future trials, which we already recommended in the discussion of our current publication in November 2014.[1]

In conclusion, we need to learn through further studies about the minimal important difference across the range of the CCI. We are looking forward to results of further studies using and discussing the CCI as an overall measure of morbidity after surgical procedures. We are convinced that so far, the CCI reflects best the overall burden of the postoperative course and mainly, represents the health of patients and their quality of life after surgery. Additionally, the CCI may allow in the future better information of patients, standardized reporting in outcome research, and increased comparability and benchmarking of quality of surgery across centers.

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